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CRYOTHERAPY IN THE TREATMENT OF SNAKE ENVENOMATION

by

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SUMMARY PAGE

THE PROBLEM

To determine the effectiveness of cryotherapy in the treatment of poisonous snake envenomation using dogs as subjects.

FINDINGS

Cryotherapy tends to enhance the destructive effects of snake envenomation. The seven dogs given sublethal doses of Crotalus adamanteus venom and treated with cryotherapy to the envenomated extremity developed hemorrhagic necrosis of large areas of skin on the treated legs. The control dogs all recovered without any tissue destruction.

RECOMMENDATION

Cryotherapy should not be used in the treatment of poisonous snake envenomation.

ADMINISTRATIVE INFORMATION

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ABSTRACT

The effectiveness of cryotherapy in the treatment of poisonous snake envenomation was evaluated. Fourteen dogs were injected in their hind paws with 40 mg of Crotalus adamanteus venom (Eastern diamondback rattlesnake). None of the seven control dogs which received either no treatment or 20 cc of Crotalidae polyvalent antivenom had any significant tissue loss. All seven dogs that received cryotherapy to their envenomated extremity for six days developed hemorrhagic necrosis of skin on this leg. The evidence presented here suggests that cryotherapy enhances the damaging effects of poisonous snake venom on the tissue.

Cryotherapy in the Treatment of Snake Envenomation

There is a great deal of controversy regarding the use of cryotherapy in the treatment of poisonous snake envenomation. The support for cryotherapy has been based primarily on results obtained with its use in treating victims of snakebite.[1-3] Others[4-7] report that use of cryotherapy in treating poisonous snakebites increases the degree of tissue destruction. The opinions of the opponents are based both on cases they have treated and on animal experimentation. Lockhart's[8] defense against those who condemn cryotherapy is that they employ the treatment improperly. It is his contention that cryotherapy must begin as soon as possible and be continued for 6 days without interruption. During this period the skin temperature should stay between 7 and 15°C, which is cold enough to inactivate enzyme-like activity of the venom. There have been no well controlled studies using cryotherapy over a 6-day period to treat snake envenomation.

The purpose of this study is to evaluate cryotherapy, using the method of Lockhart, in the treatment of poisonous snake envenomation in dogs.

METHODS

Fifteen healthy mongrel dogs weighing between 38 and 59 pounds (average, 46 pounds) were studied (Table 1). None of the dogs had antibodies to Crotalus adamanteus (Eastern diamondback rattlesnake) venom as determined by the agar plate precipitin test.[9] Fourteen dogs were given venom. These were divided into four groups (A-D) as described below. Each of these dogs had 1 cc of n saline containing 40 mg of Crotalus adamanteus venom injected through a 25 g needle into the subcutaneous tissue of the dorsum of the left hind paw. Just prior to administration of venom each dog was anesthetized with 25 mg of pentothal sodium per kilogram. The anesthesia lasted for approximately 1 hour. The remaining dog was not injected with snake venom.

The dogs were housed in individual cages throughout the study. Photographs were taken of each dog before, during, and at the end of the treatment period. The diameters of the hocks and paws and rectal temperature of each dog were recorded at intervals throughout the observation period. Times of onset and disappearance of edema, ecchymosis, blistering and oozing of exudate were noted. The injection site was excised from each dog on the seventh day post envenomation. In addition, a biopsy was obtained from the thighs of each dog that developed gangrene above the hock joint. In dogs receiving cryotherapy it was administered by encasing the leg, up to the hock, in a loose-fitting plastic boot containing a K-pad.* The boot was filled with ice water and kept cold by

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* A flexible rubber pad, 12 x 18 inches, consisting of coils of rubber tubing through which a liquid refrigerant can be circulated.

circulating antifreeze at 31°C through the K-pad. A thermocouple was taped to the dorsum of the ankle and the skin temperature was kept between 7-15°C (44-59°F). The dogs were kept in cages (5x3½ feet) to prevent them from exercising. They lay on their right sides throughout most of the study.

Treatment

Group A (4 dogs). No specific treatment was given to these dogs.

Group B (4 dogs). Fifteen minutes post envenomation (PEV) treatment with cryotherapy began and was continued for 6 days, except for short examining periods of 3 to 5 minutes duration.

Group C (3 dogs). A ligature, sufficiently tight to obstruct the superficial venous return, was applied to the leg 3 inches above the paw 3 minutes PEV. Thirteen minutes PEV 20 cc of Crotalidae polyvalent antivenom was given intravenously in the foreleg. The tourniquet was released 1 minute after the antivenom was given. No other treatment was given.

Group D (3 dogs). Dogs in this group received the same treatment as those in Group C. In addition, beginning at 15 minutes PEV the envenomed legs were treated with cryotherapy for 6 days.

Group E (1 dog). This dog was not injected with venom. It was given cryotherapy to the left hind leg for 24 hours. Since dogs, not injected with venom, would not tolerate cryotherapy, this dog was anesthetized with pentobarbital sodium during the entire 24 hours.

RESULTS

Group A (venom without treatment). Within 15 minutes post injection, the foot became markedly edematous and ecchymosis extended 2 inches above the injection site. Edema developed so rapidly that at the end of 1 hour the diameter of the paw increased by 50% and that of the hock by 100%. Ecchymosis and edema reached their maximum extent within 24 hours, involving the entire leg, extending onto the left abdominal wall and across the midline to the right lower quadrant. A hemorrhagic bulla formed at the injection site 1 to 3 hours post envenomation from which a serosanguineous exudate began almost immediately. The exudate stopped on the second day. The dogs walked on their envenomated legs on the third or fourth day. Ecchymosis and edema faded rapidly from the third day to the seventh day post envenomation. On the seventh day the leg appeared normal except for minimal ecchymosis of the medial thigh and lower leg (Figure 1).

Group B (venom with cryotherapy). These dogs were quiet and appeared sick during the entire 7 days of the study. Edema and ecchymosis developed just as rapidly and extensively with the cryotherapy as in dogs with no treatment (Table 2). Bullae occurred at the injection sites and in one dog on the medial thigh 20 to 40 hours post injection. Oozing of serosanguineous exudate began 5 to 14 hours post envenomation and persisted for 4 to 7 days (Table 3). The dogs did not bear weight on the legs during the treatment period. On the fourth day of cryotherapy the paw and medial thigh began to appear gangrenous and slowly became more necrotic as the period of cryotherapy progressed. The edema and ecchymosis persisted through the entire treatment period. On the seventh day the paw of each dog was hemorrhagic and necrotic (Figure 2). Three of the dogs had large necrotic sloughs of the skin from the thigh (Figure 3). Biopsies revealed complete destruction of the entire thickness of the skin due to hemorrhagic necrosis. The gangrene was so extensive that three of the dogs were sacrificed.

Group C (treatment with ligation and antivenom). The swelling did not extend above the mid-stiffle area and the ecchymosis was confined to the skin of the lower leg and medial thigh. Edema reached its maximum in 12 hours and subsided completely in two dogs by the fourth day and in the other dog by the fifth day (Figure 4). There were no hemorrhagic bullae. Oozing from the injection sites occurred in only two dogs, beginning 2 hours PEV and ending within 18 hours PEV. Histologic examination of skin from the injection site was normal except for a few inflammatory cells in the subcutaneous tissue. The leg appeared normal on the seventh day PEV.

Group D (venom, ligation, antivenom and cryotherapy). These dogs appeared ill through the 7-day period following envenomation. Edema and ecchymosis developed over the entire leg and across the midline of the abdomen and persisted throughout the entire period of cryotherapy. Serosanguineous fluid oozed from the paw beginning at 4 to 20 hours PEV and ending in 48 to 92 hours PEV. Bullae of the hemorrhagic type developed on the paws of two dogs and thigh of the other. One dog had hemorrhagic necrosis of the paw only. Necrosis of the paws and medial half of the legs, up to mid-thigh level, developed in each of the other two dogs (Figures 5 and 6). The dogs started weight bearing on the envenomated extremity 12 days PEV, at which time the edema and ecchymosis had subsided. On histologic examination, there was complete hemorrhagic necrosis of tissue surrounding the biopsy sites.

Group E (cryotherapy alone for 24 hours). This dog had no change in the appearance of his paw and walked on the leg as soon as he recovered from anesthesia.

The temperature response was about the same in all of the dogs. Within 2 hours PEV rectal temperatures rose to between 102.8 and 105.0°F.

Temperatures returned to a normal range within 12 to 20 hours, and remained so during the 7-day period. With the onset of necrosis there was no corresponding temperature elevation.

The results are summarized in Table 4.

DISCUSSION

Most bites by snakes of the pit viper group result in local tissue damage but few produce fatalities.[10] In this study, cryotherapy was tested for its effect in protecting against the local destructive effects of the proteolytic and hemolytic enzymes of snake venom. Therefore, each dog was injected with 40 mg of venom which, for a dog with an average weight of 46 pounds, is approximately one-fourth the lethal dose of 8 mg/kg.[5]

Cryotherapy was given continuously over a period of 6 days. Previous experiments with cryotherapy in treating sublethal injection of venom have only used it for periods ranging from 8[5] to 36[3] hours. In spite of the long period of cryotherapy in this study, the destructive effects of venom were not inhibited. In every dog receiving cryotherapy, either in conjunction with ligation and antivenom or alone, the local tissue destruction was much greater than in the control dogs. Edema, ecchymosis, bulla formation, and oozing of serosanguineous exudate were as severe as in control dogs and much more prolonged (Tables 3 and 4). This is probably due to the prolonged contact of venom with the tissue in an extremity in which the circulation has been reduced by the use of cryotherapy. There is no evidence to suggest inactivation of venom by tissue temperature of 15°C and below.

It is unlikely for several reasons that the necrosis which developed in dogs treated with cryotherapy was due to freezing. One control dog given cryotherapy to his leg (Group E) for 24 hours showed no evidence of tissue injury. In the dogs treated with cryotherapy, necrosis developed at injection sites or proximal to the sites along the medial sides of the legs. The areas of necrosis correlated well with the course of lymphatic drainage from the injection sites and with the locations of the most intense ecchymosis in the untreated controls. There was no necrosis in paws distal to injection sites or on the lateral or posterior aspects of the legs. Additionally, the extent and degree of necrosis in the dogs of Group B, treated with cryotherapy alone, was much greater than in Group C, where antivenom was used in conjunction with cryotherapy.

Hemorrhagic necrosis resulting in loss of tissue from the involved leg of each dog receiving cryotherapy is strong evidence against the use of cryotherapy in treating envenomation by poisonous snakes of the pit viper group; not

only is tissue destruction increased but the period of disability is lengthened. The evidence presented in this paper confirms the observations of those who condemn the use of cryotherapy in the treatment of poisonous snakebite.

CONCLUSIONS

Cryotherapy in the treatment of envenomation with sublethal doses of Crotalus adamanteus venom was studied in dogs. Some dogs were treated only by cryotherapy and others with cryotherapy in conjunction with ligation and antivenom. The results have led to the following conclusions:

1. Cryotherapy does not inactivate the damaging effects of poisonous snake venom.

2. The degree of tissue destruction is increased markedly by the use of cryotherapy.

3. Cryotherapy should not be used in the treatment of envenomation by poisonous snakes of the pit viper groups.

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Table 1

Weight, Age, Sex of Dogs Given 40 mg

of Crotalus adamanteus Venom

Group	Dog No.	Weight (lb)	Sex	Age (yr)
A	1	42	M	4
	2	40	M	3
	3	38	F	2
	4	40	F	4
B	1	44	F	2.5
	2	41	F	2.5
	3	49	F	3.5
	4	42	F	3
C	1	49	F	3
	2	54	M	4
	3	51	M	3.5
D	1	55	M	3
	2	50	M	5
	3	51	M	3.5

Table 2

Edema in Leg Injected with 40 mg of *Crotalus adamanteus* Venom

Table 3

Oozing of Serosanguineous Exudate from Leg Injected with 40 mg of Snake Venom

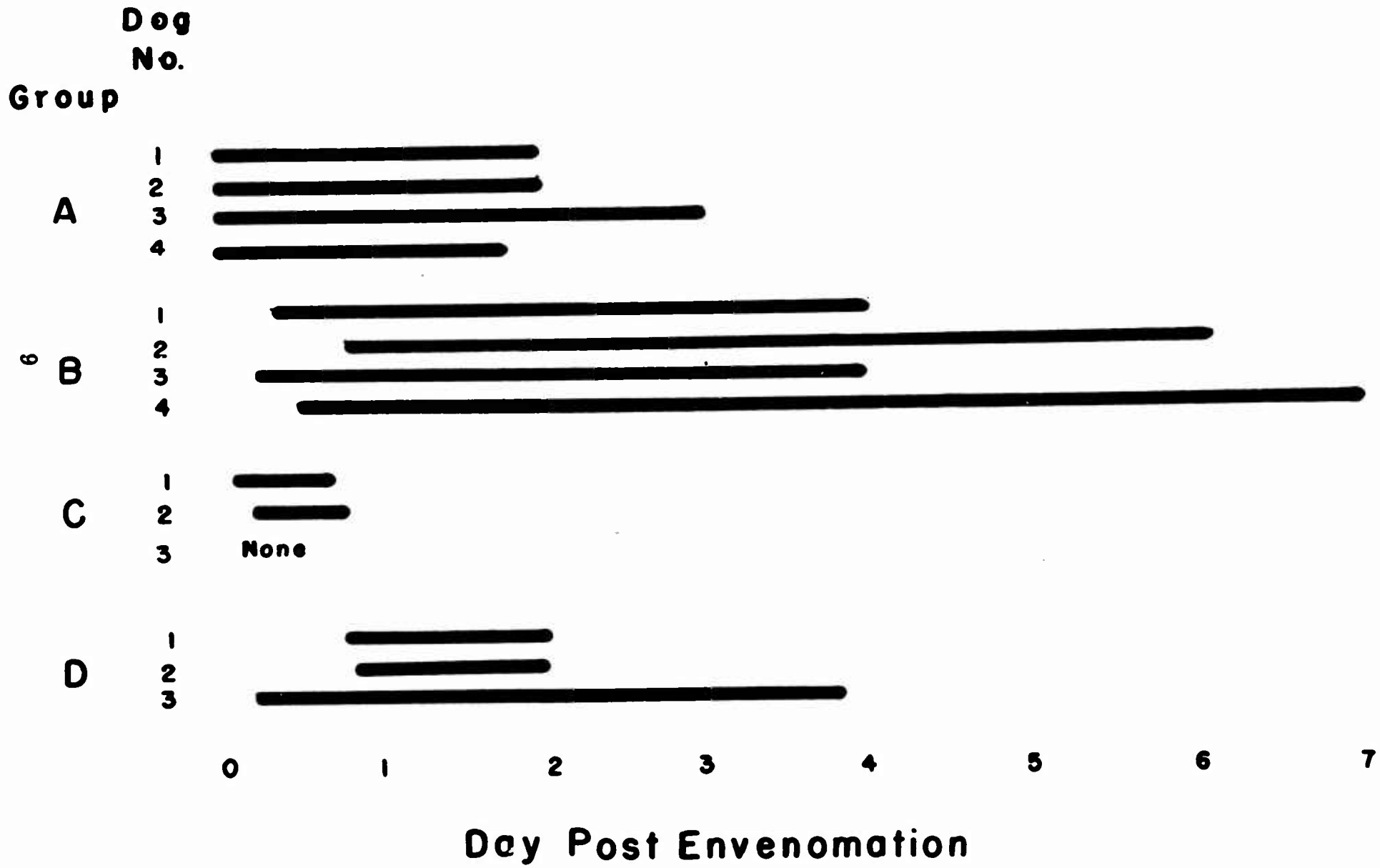

Table 4

Results of Treatment on Dogs Injected with 40 mg of Crotalus adamanteus Venom into the Subcutaneous Tissue of the Dorsum of the Hind Paw

Treatment	Group No.	Dog No.	Resumed Weight Bearing (Day PEV)	Tissue Damage on 7th Day PEV
None	A	1	2	None
		2	2	None
		3	2	None
		4	2	None
Cryotherapy for 6 days	B	1	10	Necrosis of dorsum of paw
		2	-	Necrosis of paw, medial leg and thigh
		3	-	Necrosis of paw, medial leg and thigh
		4	-	Necrosis of paw, medial leg and thigh
Ligation and 20 cc Antivenom	C	1	1	None
		2	1	None
		3	1½	None
Ligation 20 cc Antivenom and cryotherapy for 6 days	D	1	12	Necrosis of paw and medial leg
		2	12	Necrosis of paw and medial leg
		3	5	Necrosis of paw and medial leg

Fig. 1. Paw of dog #2, Group A, 7 days post envenomation. No treatment.

Fig. 2. Paw of dog #2, Group B, 10 days post envenomation. Treated for 6 days with cryotherapy.

Fig. 3. Thigh of dog #3, Group B, 7 days post envenomation. Treated for 6 days with cryotherapy.

Fig. 4. Paw of dog #3, Group C, 4 days post envenomation. Treated with ligature and antivenom.

Fig. 5. Paw of dog #2, Group D, 12 days post envenomation. Treated with ligature, antivenom and cryotherapy for 6 days.

Fig. 6. Thigh of dog #2, Group D, 12 days post envenomation. Treated with ligature, antivenom and cryotherapy for 6 days.

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13. ABSTRACT

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SUMMARY PAGE

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FINDINGS

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The experiments reported herein were conducted according to the principles enunciated in "Guide for Laboratory Animal Facilities and Care" prepared by the Committee on the Guide for Laboratory Animal Resources, National Academy of Sciences-National Research Council.

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